

REMARKS

Reconsideration of the rejection of all claims is respectfully requested in view of the above amendments and the following remarks.

Claim Status

Claim 13 is allowed. Claims 10-12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. Claims 1-4 and 15 were previously cancelled, and claims 5-9, 14, and 16-19 are rejected.

Claim Amendments

Claims 9 and 19 have been amended to remove the parenthetical definitions as an accommodation to the Examiner. As explained in the previous response, it is submitted that the parenthetical phrases were used effectively in these claim to distinguish sub-sets of definitions, *i.e.*, definitions of variables introduced by the preceding variable definition. Nevertheless, in applicants' continuing effort to advance this application to allowance, the Examiner's request has been complied with, and all parenthetical definitions have been removed and replaced by commas. No other claim amendments have been made.

These amendments are not intended to change the meaning of these claims in any respect, and therefore no new matter has been added. Since these amendments were made pursuant to a specific request by the Examiner, entry of these amendments after Final Rejection is appropriate, and entry of the same is respectfully requested.

Following entry of these claim amendments, claims 5-14 and 16-19 remain pending in this application.

Claim Rejections - 35 USC § 112, Second Paragraph

The rejection of claims 9 and 19 as being indefinite by reason of the use parentheses to more clearly delineate moiety sub-definitions and definitions has been obviated by the

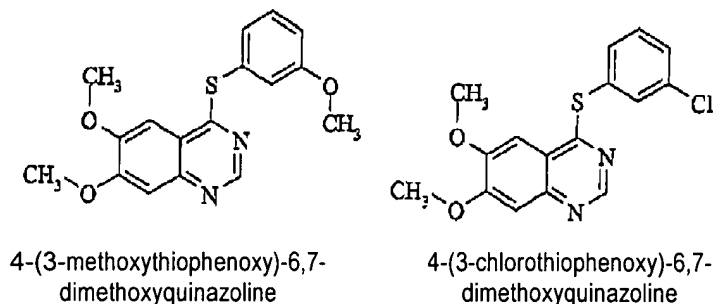
removal of these parentheses from claim 9 and 19 by the above amendments. It is respectfully requested that this ground for rejection be withdrawn.

Claim Rejections - 35 USC § 103- Myers '969 & Hawley's

Claims 5-9, 14, 18 and 19 remain rejected under 35 U.S.C. § 103 as being unpatentable over Myers et al. in view of *Hawley's Condensed Chemical Dictionary*. The rejection is said to be maintained "for the reasons stated in the previous action **and for the one below.**" Applicants refuted the Examiner's "reasons stated in the previous action" with a detailed analysis and supporting documentation at pages 18-23 of their Amendment and Response dated August 10, 2005. However, the Examiner does not address Applicants analysis and supporting documents in the current Action. Instead, the Examiner purports to have discredited Applicants construction of the term "thiophenoxy" in Myers *et al.* on the bases of the new reason she asserts for her interpretation -- the new reason characterized as "**the one below.**" However, as will be shown below, this new reason characterized as "the one below" *is itself erroneous* and in no way supportive of her *prima facie* obviousness determination.

This portion of the Final Action at pages 3 and 4 reads as follows:

In applicants' view, two of Myers' disclosed compounds (on column 9, lines 54 and 58) have the following structures:



Applicants interpreted the substituent *3-methoxythiophenoxy* to be *3-methoxyphenyl-S-*, and the substituent *3-chlorothiophenoxy* - to be *3-chlorophenyl-S-*. Applicants asserted that the term "thiophenol" in *Hawley's Condensed Chemical Dictionary*

supported such an interpretation. Note, the compound drawn on the right is **actually disclosed on column 10, line 39 of US'969** by the name of **4-(3-chlorophenylthio)-6,7-dimethoxyquinazoline**.

Therefore, applicant's interpretation of the term "*thiophenoxy*" as *phenyl-S-* is not the meaning intended by Myers et. al.

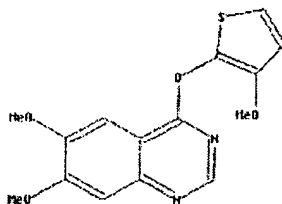
(Action at pages 3-4).

A fundamental flaw in the Examiner's analysis, however, is that the "compound drawn on the right" **is not** the compound disclosed on column 10, line 39 of Myers '969. The compound disclosed in column 10, line 39 of Myers '969 is 4-(3-chlorophenylthio)-6,7-**dimethyl**quinazoline, whereas the "compound drawn on the right" is a 6,7-**dimethoxy**quinazoline. The "compound drawn on the right" is *exactly* disclosed at column 9, line 58 of Myers '969 as "4-(3-chlorothiophenoxy)-6,7-dimethoxyquinazoline," and the compound drawn to the left is *exactly* disclosed at column 9, line 54 of Myers '969 as "4-(3-methoxythiophenoxy)-6,7-dimethoxyquinazoline."

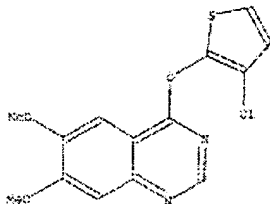
The remainder of the Examiner's discussion of Myers '969 is a series of unsupported conclusory statements drawn from her prior Action and/or based on the erroneous premise noted above:

As discussed in the previous action the term "thiophenol" denotes a moiety of *phenyl-SH* (the thiol group is a terminal group), and is equivalent to the name "*phenyl mercaptan*". Therefore, the term "thiophenol" does not support applicants' interpretation of *thiophenoxy* as *phenyl-S-*. Furthermore, as pointed out in the previous action, on column 3, Myers et. al. list the preferred heteroaryl rings including *thiophene* (see column 3, line 41). Also, on column 10, Myers et. al. disclose a compound having the substituent of *3-chlorophenylthio* (see column 10, line 39), which is *3-chlorophenyl-S-*. Clearly, Myers et. al. intend *thiophenoxy* to be **thiophen-O-**, and not *phenyl-S-* as suggested by applicants.

That is, the compound of 4-(3-methoxythiophenoxy)-6,7-dimethoxyquinazoline has the structure of :



and, the compound of 4-(3-chlorothiophenoxy)-6,7-dimethoxyquinazoline has the structure of:



Thus, the generic teaching of Myers et. al. still renders obvious compounds of the instant formula II because it teaches a substituted *thiophenoxy* group which corresponds to a group represented by the instant variables Zb-(ring C)-(R¹)_n. It also provides equivalent teaching for many substituents (corresponding to the instant R² and R^{2a}).

(Action at pages 4-5).

The Examiner makes no mention of the arguments and supporting documents refuting those conclusions presented by Applicants' in their August 10, 2005 Amendment and Response. Under the circumstances, those prior argument bear repeating.

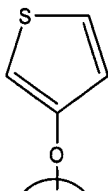
Accordingly, as will be shown again below, the Examiner has not met her burden of establishing *prima facie* obvious based on Myers *et al.* in view of *Hawley's Condensed Chemical Dictionary*.

The section 103 obviousness rejection over Myers *et al.* has been based on the Examiner's assertion that the term "thiophenoxy" used in two Myers '969 compounds denotes a "thiophene" ring attached to the quinazoline via an oxygen linker. To the contrary, Applicants have demonstrated that whether one construes the term "thiophenoxy" by its old common meaning or tries to interpret this term in context of more modern nomenclature, under no circumstances would "thiophenoxy" be construed as having a 5-membered heterocyclic "thiophene" ring rather than a phenyl ring, and this is confirmed as well by the definition in *Hawley's Condensed Chemical Dictionary* relied upon by the Examiner.

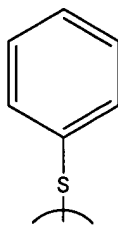
This ground for rejection is respectfully traversed for the reason, *inter alia*, that under any technically plausible interpretation of the term "thiophenoxy," in context of both old and modern nomenclature, the ring in "thiophenoxy" is *not a thiophene ring*, but rather is a phenyl ring. This is clear from the *Hawley's* definition cited by the Examiner and from the

IUPAC excerpt and other materials discussed below, and is consistent with the overall disclosure of Myers '969.

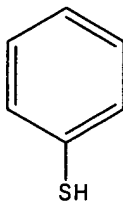
It is understood that the Examiner is asserting that the term “thiophenoxy” has the structure:



The Examiner offers nothing in support the above construction, but only attempts to refute Applicants' observation that “thiophenoxy” is the older commonly used term for the group “thiophenyl,” wherein a **phenyl** ring (rather than a thiophene ring) is linked to the 4-position via sulfur:



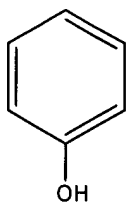
The Examiner cites *Hawley's* definition of the term “thiophenol” as being the same as the term “phenyl mercaptan”, which it lists as C_6H_5SH , *i.e.*:



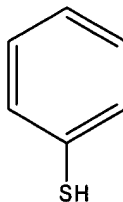
and does not list a definition for “thiophenoxy” as thiophenyl as suggested by applicant.

The point of this argument is not understood, in that it neither supports the Examiner's interpretation nor refutes Applicants' interpretation. *Hawley* and the Examiner are discussing “thiophenol,” a complete compound, whereas Applicants are discussing “thiophenyl” and “thiophenoxy,” both being radicals or portions of a larger compound.

Note *Hawley's* definition of “thiophenol” compared to “phenol”:



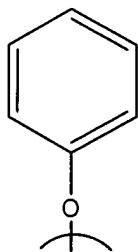
phenol



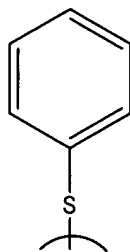
thiophenol

where, in the “O” in the phenol is substituted by an analogously placed “S” in the thiophenol. In this older terminology, the thiophenol is *not* a phenol on which a thio “SH” group is additionally placed elsewhere on the ring, but rather the thiophenol substitutes the “O” of the phenol with an “S”.

In an analogous manner, the radicals (molecule portions) denoted by the terms “phenoxy” and “thiophenoxy” have the following structures:



phenoxy



thiophenoxy

where the “O” in the phenoxy group is substituted by an analogously placed “S” in the thiophenoxy group, consistent with Applicants’ interpretation, and not at all supportive of the Examiner’s assertion that the phenyl ring in phenoxy and thiophenoxy has somehow been transformed to a “thiophene” ring.

Support for the above analysis and conclusions, and refutation of the Examiner’s unsupported assertion that a “thiophene” ring is somehow involved, is found, *inter alia*, in the “Thiols and Related Compounds” Section C-5.1 of the IUPAC “Nomenclature of Organic Chemistry,” 1995 printing. A copy of the title page and Section C-5.1 (pages 211-217) was submitted with the Amendment and Response filed August 10, 2005.

Attention is first drawn to page 212, Rule 511.2, which states, “The use of ‘thio-’ prefixed to the trivial name of a phenol, indicating replacement of the hydroxylic oxygen by sulfur, may be continued in simple instances, but the nomenclature of Rule C-511.1 is

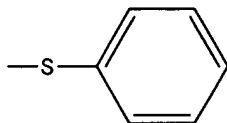
preferred.” (Emphasis added). Rule C-511.1 provides the more modern nomenclature, stating in part, “When --SH is not the principal group, the prefix ‘mercapto-’ is placed before the name of the parent compound to denote an unsubstituted --SH group.” Note also footnote * stating that “The class name ‘mercaptan’ is abandoned. The root is retained only in the prefix ‘mercapto-’ for an unsubstituted --SH group.”

The text of IUPAC Rule C-511.1 also states, “Note: ‘Thiol’ is not to be confused with ‘thiole’ which denotes a five-membered ring embodying one sulfur atom.” (Emphasis added). It appears that this may be what the Examiner has done.

Other uses in the art consistent with Applicants’ interpretation of the term “thiophenoxy” include:

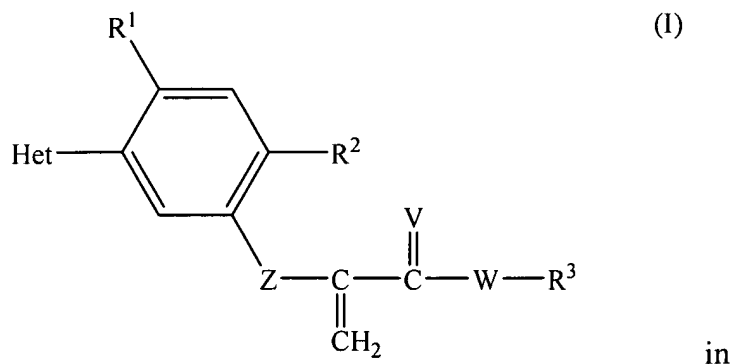
- US Patent 5,055,569, issued October 8, 1991, stating at column 7, lines 14-20:

For the purpose herein the term “thiophenoxy” is used to mean the group having the structure:



- US Patent 6,528,455, issued March 4, 2003 based on an International Application filed December 15, 2000, published January 5, 2002, claiming priority from December 16, 1999, clearly demonstrates use of nomenclature in precisely the period in which the present invention was made. This patent is entitled, “PHENOXY- AND THIOPHENOXY ACRYLIC ACID COMPOUNDS AS HERBICIDES.” At column 1, lines 6-22, it is stated:

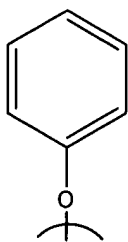
The present invention relates to 2-phenoxy- and 2-thiophenoxyacrylic acid compounds of the formula I



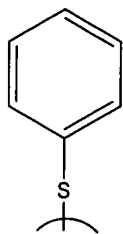
which

Z, V and W independently of one another are oxygen or sulfur, . . .

In other words, when Z is oxygen, the structure represents a 2-phenoxyacrylic acid compound, and when Z is sulfur (the only alternative), the structure represents a 2-thiophenoxyacrylic acid compound. It is thus absolutely clear from this reference that common usage at the time of the present invention denoted the radical:

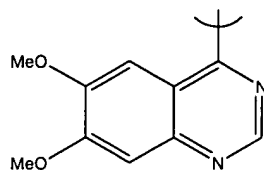


a phenoxy group (*i.e.*, Z is oxygen) and, consistently therewith, the radical:

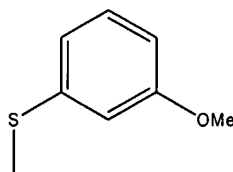
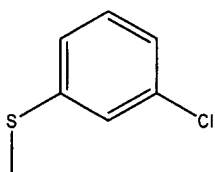


a thiophenoxy group (*i.e.*, Z is sulfur).

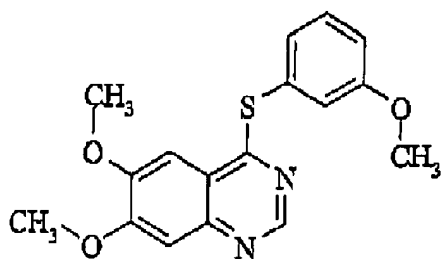
It is therefore respectfully submitted that it is clear from the above that the compounds *named* in Myers '969 at column 9, line 54 (4-(3-methoxythiophenoxy)-6,7-dimethoxyquinazoline) and line 58 (4-(3-chlorothiophenoxy)-6,7-dimethoxyquinazoline) *correspond exactly to the structures shown at Myers '969 in column 15, lines 45-50 and lines 51-56*, wherein the base quinazoline structure for both compounds is:



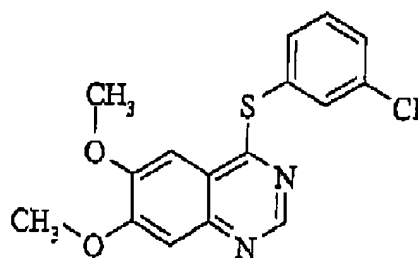
as shown at the top of column 15, and the 4-position substituents have the structures:



respectively. Piecing the 4-position substituent with the quinazoline base structure, it can be seen that the compounds *named* at column 9, lines 54 and 58, have the following structures:



4-(3-methoxythiophenoxy)-6,7-dimethoxyquinazoline



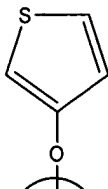
4-(3-chlorothiophenoxy)-6,7-dimethoxyquinazoline

respectively, and very clearly do not have a thiophene ring anywhere in the 4-position substituent on the quinazoline ring.

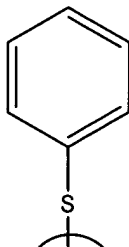
In the present Action the Examiner advances a new reason said to support her construction, that is, that "the compound drawn on the right is **actually disclosed on column 10, line 39 of US'969** by the name of **4-(3-chlorophenylthio)-6,7-dimethoxyquinazoline**"

(emphasis in original), from which the Examiner concludes that Myers '969 intended *thiophenoxy* to be **thiophene-O-**, and not *phenyl-S-* as suggested by applicants. However, as noted above the compound drawn to the right is not the compound 4-(3-chlorophenylthio)-6,7-dimethoxyquinazoline, as should be readily apparent to the Examiner inasmuch as the illustrated compound to the right is 6,7-**dimethoxy** substituted quinazoline whereas the compound the Examiner points to is 6,7-**dimethyl** substituted. In other words, Applicants interpretation of the structure of the compounds 4-(3-methoxythiophenoxy)-6,7-dimethoxyquinazoline and 4-(3-chlorothiophenoxy)-6,7-dimethoxyquinazoline is confirmed by an exact match with the Myers '969 structure as shown above, whereas there is no structure disclosed in Myers '969 that matches the compound now advanced by the Examiner in support of her construction.

In short, there remains **no support** for the Examiner's asserted construction of the term "thiophenoxy" as having the structure:



whereas there is direct support in the Myers '969 reference itself for Applicants "thiophenoxy" structure" as being:



which construction is supported by and/or at least consistent with the other patents cited above as well as *Hawley's Condensed Chemical Dictionary* and the passages from IUPAC discussed above.

Accordingly, the Examiner has not met her burden of establishing *prima facie* obviousness over Myers '969, and this ground for rejection should be withdrawn.

Claim Rejections - 35 USC § 103- Myers '969 & Mohammadi

The continuing rejection of claims 16 and 17 over Myers '969 in view of Mohammadi is premised on the same misconceptions with respect to the structure of the two Myers '969 compounds, and therefore this ground for rejection should be withdrawn as well. While Applicants disagree with the Examiner's assertion that Mohammadi would somehow expand the very clear use taught by Myers '969 (*i.e.*, inhibition of the colony stimulating factor-1 receptor tyrosine kinase, CSF-1R, activity) to suggest Applicants' quite different method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal, this issue is now moot and need not be addressed at this time. It is well established that a composition containing, or a method using, a novel and unobvious compound would also be novel and unobvious be reason of the patentability of the compound claims.

Claim Rejections - 35 USC § 103 - Manning WO '321

The rejection of claims 5-9 and 18 as being unpatentable over Manning *et al.*, WO 87/04321 under section 103(a) has been maintained for the reasons stated in the previous action. Applicants pointed out in their August 10, 2005 Amendment and Response that this reference would be considered "non-analogous art" under US practice,¹ but that in any event the single compound pointed to by the Examiner (last compound on page 117) differs from the presently claimed compounds in very material respects. As will be further shown below, this is one of *only three* quinazoline compound disclosed in this extensive 791 page reference, *all* of which differ from the presently claimed compounds in material respects. In particular, the ring substituents in each of these compounds fall outside of the present claims such that *even if* there was a suggestion to mix and match the substituents in these three

¹ Manning discloses as the only use for its compounds the reduction of transpirational water loss from plants and increase of crop yield, which is an entirely different field from the specific medicinal use of the presently claimed compounds, and clearly non-analogous. However, as detailed below, the present compounds are clearly quite structurally distinct from the presently claimed compounds, and this will be the focus of the remaining remarks.

references at any position on the respective rings, one *still could not* achieve a compound within the scope of the present claims. Thus, there is no suggestion or guidance whatsoever to modify any of these three exemplified quinazoline compounds in a manner that might lead one skilled in the art to a compound within Applicants' present claims. Accordingly, the Manning *et al.* reference cannot support the *prima facie* obviousness rejection.

The Examiner's present response to Applicants previous observations and arguments is as follows:

Claims 5-9 and 18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Manning et. al.** (WO 87/04321). The rejection is maintained for the reasons stated in the previous action and for the following ones:

Applicants asserted that:

"there is no guidance in this reference that would lead the skilled person to make any compound as presently claimed....

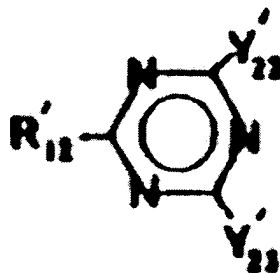
Thus, in order to make a compound within the present claim from the Manning disclosure, the skilled person must first serendipitously select the bottom compound on page 117 out of all the compounds disclosed on pages 46 to 238, for which no particular guidance or suggestion is given..."

Applicant's argument of "no guidance" or "no suggestion" is unfounded. The fact is, Manning et. al. specifically disclose a **quinazoline compound substituted with triazinyl-O-**, and provide equivalent teaching for substituents at all positions on the quinazoline ring. Such a disclosure is guidance enough. The fact is, the last compound on page 117 is very structurally analogous to a compound of the instant formula II, but differs only in the position of substituents on the *benzo* ring of the quinazoline. Such a difference can be overcome by the generic teaching of the reference.

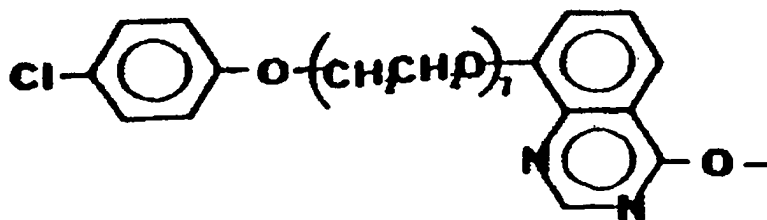
Thus, the guidance for one skilled in the art to make a quinazoline compound substituted with triazinyl-O- clearly lies in both the **species and genus** disclosed by Manning et. al.

(Action at pages 5-6). Applicants respectfully disagree with the Examiner's assertions regarding this reference and the conclusions drawn therefrom.

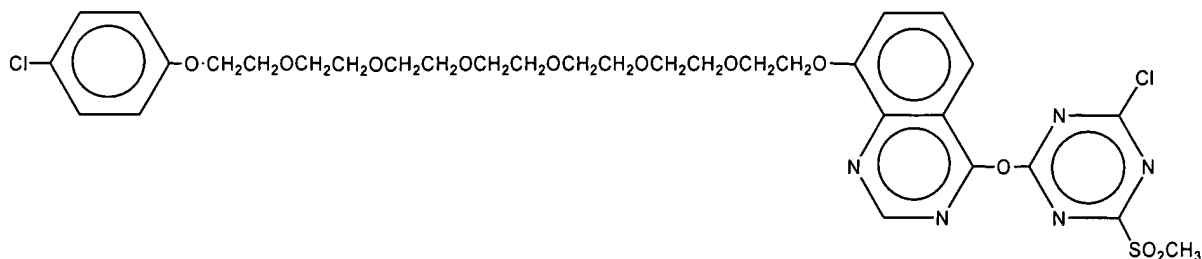
In making this rejection, the Examiner cites one compound from Table 14 (at page 117 of the Manning specification) as being "a triazolyl compound substituted with a quinazolin-oxy." The imaged structures in this reference are very difficult to read, so they will be greatly expanded below. It is believed that the compound referred to by the Examiner has the triazol ring common to the compounds of Table 14:



wherein the group R'_{12} is shown with the following structure:



and Y'_{22} is said to be Cl and Y'_{23} is said to be CH_3SO_2 . The resulting compound becomes:



The Examiner asserts in the present Action that this Manning *et al.* compound “is **very structurally analogous** to a compound of the instant formula II, but **differs only in the position of substituents on the benzo ring of the quinazoline,**” and that “such a difference can be overcome by the generic teaching of the reference.” (Emphasis added).

It should be readily apparent from a comparison of the above structure of the Manning *et al.* compound that it is **not** structurally analogous to compounds of the present claims. While the cited compound from Manning *et al.* has a 5 or 6-membered heterocyclic ring attached to the 4-position of a quinazoline ring structure via an oxygen, the present claims ***expressly preclude*** having a substituent at the 8-position of the quinazoline ring in contrast to the cited Manning *et al.* compound, which has a massive 8-position substituent.

In an attempt to diminish the significance of this distinction, the Examiner asserts that this compound “differs only in the **position** of substituents on the *benzo* ring of the quinazoline.” That is not correct. The massive Manning *et al.* 8-position substituent does not fall within the definition of ***any*** substituent on the quinazoline ring of the present application, and therefore simply moving it around the ring, as the Examiner seems to be suggesting, still does not overcome this distinction.

However, the Examiner still further asserts that “such a difference can be overcome by the generic teaching of the reference.” This also is not correct. The generic teaching of Manning *et al.* is an incredibly broad genus $R_1 - X - R_2$ wherein:

R_1 is a substituted or unsubstituted, carbocyclic or heterocyclic ring system selected from a monocyclic aromatic or nonaromatic ring system, a bicyclic aromatic or nonaromatic ring-system, a polycyclic aromatic or nonaromatic ring system, and a bridged ring

system which may be saturated or unsaturated in which the permissible substituents (Z) are the same or different...

* * * * *

X is a covalent single bond or double bond, a substituted or unsubstituted heteroatom or substituted carbon atom, or a substituted or unsubstituted, branched or straight chain containing two or more carbon atoms or heteroatoms in any combination in which the permissible substituents (Z) are the same or different...

* * * * *

R₂ is a substituted or unsubstituted, heterocyclic ring system having at least one nitrogen atom which is selected from a monocyclic aromatic or nonaromatic ring system, a bicyclic aromatic or nonaromatic ring system, a polycyclic aromatic or nonaromatic ring system, and a bridged ring system which may be saturated or unsaturated in which the permissible substituents (Z) are the same or different...

(Specification at pages 5-13).

The only guidance in this specification toward quinazoline-based compounds is found in:

- (A) the last compound on page 117 (cited by the Examiner and set out above), but this cited example differs from the present invention because:
- (i) it has a mandatory hydrogen at the 7-position (C-7) of the quinazoline ring but in claim 18 of the present application R² (C-7) cannot be hydrogen because of the proviso at the end of the definition of R²;
 - (ii) it has a very large substituent at the 8-position (C-8) but in claim 18 of the present invention C-8 can only be hydrogen, Furthermore the 4-chlorophenyl-O-(CH₂CH₂O) at the 8-position of the example does not lie within the scope of R² of the present claims, *i.e.*, it cannot be a substituent at any position of the quinazoline ring in the present application; and
 - (iii) it has a groups CH₃SO₂ and Cl on the triazine ring but neither substituent is a permitted value for R¹ in claim 18 of the present application.

(B) The two quinazoline compounds listed as the 3rd and 4th compounds on page 140 of Manning *et al.* (the first of which is repeated as the first compound on page 153 and its preparation described on page 407), being the compounds

2,4-dichloro-5-(4'-quinazolinoxy)-1,3,5-triazine; and

2,4-dichloro-8-(4'-quinazolinamino)-1,3,5-triazine

However, these two compounds also do not lie within the scope of the present invention because

- (1) they both have a mandatory hydrogen at the 7-position (C-7) of the quinazoline ring, but in claim 18 of the present application R² (C-7) cannot be hydrogen because of the proviso at the end of the definition of R²;
- (ii) they both have two chloro substituents on the triazine ring, but chloro and indeed halogeno are not permitted values for R¹ in claim 18 of the present application; and
- (iii) for the second compound the linker group is -NH- which is not a permitted value for Zb in claim 18.

For all of the above reasons, it is respectfully submitted that the Examiner has failed to make out a case of *prima facie* obviousness over the Manning *et al.* reference, and withdrawal of this ground for rejection is respectfully requested.

Again, it is respectfully submitted that there is no guidance or suggestion anywhere in this reference that would motivate the skilled person to modify any of the only three quinazoline compounds disclosed in this reference (in the unlikely event that one of these compounds was selected for modification in the first place) to make the combination of substituent replacements and ring-position changes that would be necessary to achieve any compound within the scope of Applicants present claims.

The Federal Circuit has made very clear that the burden is on the Patent and Trademark Office to establish a *prima facie* case of obviousness in the first instance. It is a fundamental principle of the patent laws that a *prima facie* case of obviousness has not been made unless it is demonstrated that persons of ordinary skill in this art would have been motivated by the prior art to select the particular claimed species or subgenus from the

disclosed prior art genus. In re Ochiai, 71F.3d 1565, 1569-70, 37 USPQ2d 1127, 1131 (Fed. Cir. 1995); Deuel, 51 F.3d at 1557, 34 USPQ2d at 1214 ("[A] prima facie case of unpatentability requires that the teachings of the prior art suggest the claimed compounds to a person of ordinary skill in the art."(emphasis in original)); Jones, 958 F.2d at 351, 21 USPQ2d at 1943-44 (Fed. Cir. 1992); In re Dillon, 919 F.2d 688, 692, 16 USPQ2d 1897,1901 (Fed. Cir. 1990)(in banc); In re Lalu, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir.1984)("The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound.").

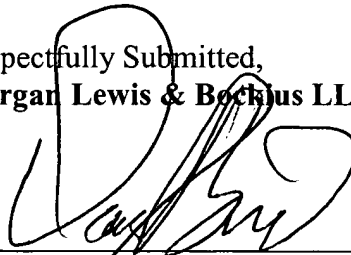
Accordingly, it is respectfully submitted that the Examiner has not met the PTO burden of establishing prima facie obviousness with respect to any of the cited references, and the rejections under 35 U.S.C. § 103 should be withdrawn.

Conclusion

It is believed that all ground for rejection have been addressed and overcome by the above Amendments and the foregoing remarks. Accordingly, withdrawal of all grounds for rejection and the allowance of all claims are respectfully requested.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully Submitted,
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